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Original Research Article

A STUDY ON THE PREVALENCE OF MICROALBUMINURIA IN NON-DIABETIC PATIENTS WITH ACUTE MYOCARDIAL INFARCTION IN ICCU

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ABSTRACT

Background: Microalbuminuria, a marker of microvascular and endothelial dysfunction, is associated with increased cardiovascular risk and mortality in non-diabetic patients with acute myocardial infarction. This study aimed to investigate the prevalence of microalbuminuria in non-diabetic patients with acute myocardial infarction (both STEMI and NSTEMI) and to study the association between microalbuminuria and other risk factors.

Material and Methods: This hospital-based cross-sectional study included 100 patients treated at the Government Vellore Medical College between October 2017 and September 2018. The patient details and covers the history of age, sex, comorbidities, personal habits, clinical examination, BMI calculation, and investigations, such as blood sugar, lipid profile, renal function tests, urine analysis, ECG, Troponin T, and echocardiography.

Results: Of the 100 patients, 61 (61%) were males and 39 (39%) were female. Of the patients, 55% had cholesterol levels (205.7±36.9) >200 mg/dL, with 50.82% males and 61.54% females. A BMI >25 was observed in 67% (26.1±2.4) of the patients, with 72.13% males and 58.97% females. Triglyceride levels >150 mg/dL were noted in 57 patients (160.3±34), 59.02% males and 58.97% females. Among the 51 (51%) patients who smoked, all 51 smokers were male. Microalbuminuria (ACR ≥ 30 mg/g) was present in 64% of the patients, with significant differences in cholesterol, BMI, and triglycerides between the ACR groups ($p = 0.0005$, $p = 0.02$, $p = 0.0004$).

Conclusion: Microalbuminuria was prevalent in 64% of patients with acute myocardial infarction, with higher rates in younger patients. It is strongly associated with dyslipidaemia, elevated cholesterol, triglycerides, and high BMI but can occur independently of BMI, smoking, and cholesterol levels.

Keywords: Microalbuminuria, Acute Myocardial Infarction, Non-diabetic, Dyslipidaemia, Endothelial dysfunction.

INTRODUCTION

Coronary artery disease (CAD) is one of the most common diseases in hospitalized patients in industrialized countries. The mortality rate in patients with acute myocardial infarction is approximately 30%. One of the 25 patients who survived acute myocardial infarction died within the first year after acute myocardial infarction. Many factors, such as age, diabetes mellitus, and heart failure can adversely affect the prognosis of patients with acute myocardial infarction.[1] Multiple new biomarkers of coronary artery disease have been identified, including increased lipoprotein A, Total plasma homocysteine levels, elevated fibrinogen levels, C-reactive protein levels, and microalbuminuria. In patients with microalbuminuria without diabetes mellitus, vascular permeability is increased due to alterations in the extracellular matrix, contributing to the development of endothelial dysfunction, which promotes the influx of lipoatherogenic proteins into

the vessel wall, causing atherosclerotic changes. Increased albumin excretion in urine signals increased capillary leakiness for albumin and is therefore a marker of microvascular disease.[2]

Microalbuminuria is the excretion of albumin in the urine at 20-200 g (30-300 mg/dl). Routine urine tests cannot detect this range of albumin levels in the urine. Microalbuminuria has been known to be associated with diabetes mellitus. In patients with type I diabetes, microalbuminuria occurs five years after onset. Microalbuminuria is a marker for diabetic nephropathy. The patient later developed overt nephropathy.[3] In India, the incidence of coronary artery disease has increased over the last few decades, and it is equally important that Indian immigrants have a higher incidence of coronary artery disease than the native population. Cardiovascular disease occurs earlier in these patients than in the native population, that is, before the age of 40 years, even in the absence of hypertension, smoking, or hypercholesterolemia. In the last century, microalbuminuria has been studied as a predictor of incipient nephropathy and cardiovascular disease in the diabetic population.[4]

Microalbuminuria is also a sensitive marker of non-renal diseases. Parving et al. demonstrated microalbuminuria in patients with essential hypertension. In essential hypertension, microalbuminuria occurs because of an increased trans-glomerular leak of albumin. Recently, it has been shown that microalbuminuria is associated with cardiovascular disease, even in the non-diabetic population. Microalbuminuria also occurs in response to acute inflammatory conditions, such as trauma, ischemia, surgery, thermal injury, pancreatitis, and inflammatory bowel disease. In all these inflammatory conditions, the degree of microalbuminuria is directly proportional to the severity of the inflammatory insult, predictive of outcome, and not associated with any other features of renal impairment.[5]

In a cross-sectional study conducted in 2002, microalbuminuria was demonstrated to be associated with carotid intima-medial thickening, indicating that microalbuminuria is an independent risk factor for cardiovascular disease and a predictor of cardiovascular mortality.[6] It is important to know the association between microalbuminuria and cardiovascular disease because morbidity and mortality due to cardiovascular disease are increasing. Most importantly, microalbuminuria occurs in acute myocardial infarction as an early response to ischemia and is proportional to the infarct size.[7] Berton et al. demonstrated that microalbuminuria develops early in acute myocardial infarction and it is a predictor of early mortality.[8]

Aim

This study aimed to investigate the prevalence of microalbuminuria in non-diabetic patients with acute myocardial infarction (both STEMI and NSTEMI) and to study the association between microalbuminuria and other risk factors for coronary artery disease, such as hypertension, smoking, and dyslipidaemia.

MATERIALS AND METHODS

This hospital-based cross-sectional study included 100 patients with acute myocardial infarction diagnosed by clinical examination, ECG, cardiac biomarkers, and ECHO in the Department of Cardiology and Biochemistry at the ICCU of the Government Vellore Medical College between October 2017 and September 2018. This study was approved by the Institutional Ethics Committee before initiation, and informed consent was obtained from all patients.

Inclusion Criteria

Patients with acute myocardial infarction, both STEMI and NSTEMI, were clinically diagnosed, and ECG, cardiac biomarkers, and ECHO were included.

Exclusion Criteria

Patients with diabetes mellitus, hypertensive patients taking ACE/ARB, urinary tract infection, acute febrile illness, serum creatinine > 2 mg/dl, and chronic kidney disease were excluded.

Methods

The selected patients were studied in detail, beginning with a comprehensive history and physical examination to document characteristics, such as age and sex. Presenting complaints were noted along with past medical history, including diabetes, hypertension, chronic kidney disease, and epilepsy. Personal history including smoking, alcohol consumption, and bladder and bowel habits was recorded. A complete clinical examination was conducted to assess complications, and weight and height were measured to calculate the body mass index using the formula weight (kg)/height (m^2). All patients underwent the following investigations: random blood sugar (fasting and postprandial levels, if needed), fasting lipid profile, blood urea, serum creatinine levels, routine urine examination, electrocardiogram, Troponin T assay, and echocardiography.

Estimation of microalbuminuria

Microalbuminuria was assessed using an immunoturbidimetric assay. An early morning urine sample was added, undiluted, to a buffer containing an antibody specific to human serum albumin. The reaction formed a turbid solution and the absorbance at 340 nm was proportional to the albumin concentration. A standard curve was used to determine the albumin concentration in the sample. The assay used a buffer containing polyethylene glycol (6%), Tris-HCl (20 mmol/L, pH 7.4), sodium chloride (150 mmol/L), and an anti-human albumin antibody reagent. In this procedure, 500 µL of reagent buffer was mixed with 50 µL of the standard or sample in micro cuvettes. After the initial absorbance (A1) was measured, 50 µL of the

antibody was added and the mixture was incubated at 15-20°C for 30 min. The final absorbance (A2) was recorded, and the albumin concentration was calculated.

Estimation of urine creatinine

Urine creatinine estimation was performed using the modified Jaffe's alkaline picrate method. In this method, creatinine reacts with picrate ions in an alkaline medium to form an orange-red colour complex. The absorbance of the complex, which is directly proportional to the creatinine concentration, was measured photometrically at 505 nm. The reagents included picric acid (25.6 mmol/L), sodium hydroxide (95 mmol/L), and creatinine standard (2 mg/dL). Urine samples were diluted with normal saline in a 1:50 ratio. The working reagent (1000 µL) was mixed with 100 µL of distilled water (blank), standard, or diluted urine samples. The absorbance was measured at 20 s and again at 80 s.[9]

Estimation of glucose

Glucose levels were estimated using the Bx ECO-PAK GOD/POD method. In this enzymatic reaction, glucose is oxidized by glucose oxidase to produce d-gluconic acid and hydrogen peroxide. Peroxidase (POD) then catalyses the reaction between hydrogen peroxide, 4-amino antipyrine, and phenol to form a red quinonimine dye. The intensity of the red colour, measured photometrically at 505 nm, is directly proportional to the glucose concentration in the sample. The reagents included phosphate buffer (120 mM/L), glucose oxidase (>5000 IU/L), peroxidase (1050 IU/L), 4-amino antipyrine (0.20 mM/L), phenol (11 mM/L), and standard glucose solution (100%). In this procedure, 1.0 mL of the working reagent was mixed with 10 µL of distilled water (blank), standard, or plasma sample. After incubation at 37°C for 15 min, the absorbance was measured. Normal fasting glucose levels are 70–110 mg/dL, and postprandial levels are <140 mg/dL; higher values indicate impaired glucose tolerance or diabetes mellitus (DM).[10]

Estimation of serum creatinine

Serum creatinine estimation was conducted using Jaffe's alkaline picrate method. In this method, picric acid reacts with creatinine in an alkaline medium to produce a red complex. The absorbance of this complex, directly proportional to the creatinine concentration, was measured photometrically. Non-creatinine chromogens may also react, resulting in falsely elevated levels. To counter this, sulfuric acid was added, leaving non-creatinine chromogens unaffected, and the difference in absorbance provided an accurate measure of creatinine. The reagents used included picric acid, sodium hydroxide, and a standard.

Estimation of blood urea

Blood urea was estimated using the DAM (diacetyl monoxime) method. In this reaction, urea condenses with diacetyl monoxime in an acidic medium to form a coloured complex, the intensity of which increases upon the addition of calcium salts and thiosemicarbazone. The colour intensity is directly proportional to the urea concentration. The reagents included urea reagent, diacetyl monoxime, and a urea standard.

Statistical Analysis

Data are presented as mean, standard deviation, frequency, and percentage. Categorical variables were compared using Pearson's chi-square test and ANOVA. Significance was defined as $p < 0.05$, using a two-tailed test. Data analysis was performed using IBM-SPSS version 21.0 (IBM-SPSS Corp., Armonk, NY, USA).

RESULTS

Among the 100 patients, 61 (61%) were male and 39 (39%) were female. The mean cholesterol value was 205.7 ± 36.9, BMI value was 26.1 ± 2.4 and triglyceride value was 160.3 ± 34. Of the 55 (55%) patients, cholesterol levels were > 200 mg/dl, of whom 31 (50.82%) were males and 24 (61.54%) were females. Of the patients, 67 (67%) had a body mass index > 25, of which 44 (72.13%) were male and 23 (58.97%) were female. Of the patients, 57 had triglyceride levels >150 mg/dl, of whom 36 (59.02%) were males and 23 (58.97%) were females. Among the 51 (51%) patients who smoked, all were males. [Table 1]

Among 64 (64%) patients with microalbuminuria (ACR ≥ 30 mg/g), 42 (56.41%) were male and 22 (56.41%) were female. A higher percentage of patients with cholesterol > 200 mg/dl had ACR ≥ 30 mg/g 41 (74.55%) than those with cholesterol <200 mg/dl 23 (51.11%). Among smokers, 35 (68.63%) had an ACR ≥ 30 mg/g compared with 29 (59.18%) non-smokers. More patients with BMI > 25 had ACR ≥30 mg/g 41 (71.64%) than those with BMI < 25 16 (48.48%), and more patients with triglyceride levels > 150 mg/dl had ACR ≥ 30 mg/g 46 (77.97%) than those with triglyceride levels < 150 mg/dl 18 (43.90%). There were significant differences in cholesterol, BMI, and triglyceride levels between the ACR groups ($p = 0.0005$, $p = 0.02$, and $p = 0.0004$, respectively). [Table 2]

Table 1: Distribution of cholesterol, BMI, triglycerides, and smoking status by gender

		Gender	
		Male	**Female**
Cholesterol (mg/dl)	> 200	31 (50.82%)	24 (61.54%)
	< 200	30 (49.18%)	15 (38.46%)
BMI (kg/m^2)	> 25	44 (72.13%)	23 (58.97%)
	< 25	17 (27.87%)	16 (41.03%)

Triglycerides (mg/dl)	>150	36 (59.02%)	23 (58.97%)
	<150	25 (40.03%)	16 (41.03%)
Smoking status	Yes	51 (83.61%)	0
	No	10 (16.39%)	39 (100%)

Table 2: Comparison of patient characteristics and laboratory parameters between ACR

		ACR		P value
		≥ 30mg/g	< 30mg/g	
Sex	Male	42 (56.41%)	19 (31.15%)	0.206
	Female	22 (56.41%)	17 (43.595)	
Cholesterol (mg/dl)	> 200	41 (74.55%)	14 (25.45%)	0.005
	< 200	23 (51.11%)	22 (48.89%)	
Smoking	Yes	35 (68.63%)	16 (31.37%)	0.33
	No	29 (59.18%)	20 (40.82%)	
BMI	> 25	48 (71.64%)	19 (28.36%)	0.02
	< 25	16 (48.48%)	17 (51.52%)	
Triglyceride (mg/dl)	> 150	46 (77.97%)	13 (22.03%)	0.0004
	< 150	18 (43.90%)	23 (56.10%)	

DISCUSSION

In our study, normal renal function (urea ≤ 30mg/dl, creatinine ≤ 1.1mg/dl). Therefore, microalbuminuria was not associated with renal dysfunction. This study agrees that microalbuminuria occurs in significant numbers in acute myocardial infarction and is not diabetic. Goling et al. considered microalbuminuria a sensitive indicator of non-renal disease and considered microalbuminuria a risk indicator of cardiovascular disease, and they felt that more studies are required to confirm this.[11] Haffner et al. considered microalbuminuria as a risk factor for cardiovascular disease in non-diabetic patients.[12]

Microalbuminuria in patients without diabetes could be an overwhelming response secondary to acute myocardial infarction. However, there is no ambiguity regarding the fact that microalbuminuria is significantly related to cardiovascular disease, even in non-diabetic patients. Many studies have indicated that microalbuminuria occurs in non-diabetic non-hypertensive patients and the general population, and it is an independent risk indicator in this group of patients with cardiovascular disease. Lioudaki et al. demonstrated a microalbuminuria prevalence rate of 6.6% in non-diabetic and non-hypertensive patients.[13] However, Romunstadt et al. considered other risk factors and markers to influence microalbuminuria in non-diabetic and non-hypertensive populations with a total risk of cardiovascular disease compared to those with low total cardiovascular risk.[14] Hallan et al. found a 5.2% incidence of microalbuminuria in males and 4.7% in females among non-diabetic and non-hypertensive patients. However, they concluded that the cut-off level of microalbuminuria for cardiovascular disease remains to be defined.[15]

Our study found microalbuminuria in 64 (64%) patients. The mean ACR value was 54.6 ± 41.5. This shows that the prevalence of microalbuminuria is high among patients with acute myocardial infarction, even in non-diabetic patients, and is significantly associated with coronary artery disease. Taskiran et al. also noted an association between microalbuminuria and acute myocardial infarction.[16]

In our study, 64 (64%) patients had microalbuminuria (ACR ≥ 30 mg/g), of which 42 (56.41%) were male and 22 (56.41%) were female. There were significant differences in the cholesterol, BMI, and triglyceride levels between the ACR groups ($p = 0.0005$, $p = 0.02$, and $p = 0.0004$, respectively). In Agarwall et al., the adjusted odds ratio for subclinical obesity per 1 kg of reduced lean body mass by ADP was 1.14 (95% CI: 1.06 to 1.23; $p < 0.001$).[17] In the Tien et al. study, TG was found by logistic regression to be significantly associated with micro/macroalbuminuria in our unadjusted model [odds ratio (OR) = 1.859 (1.596~2.165)], and remained significant after adjusting for various confounders [OR = 1.415 (1.123~1.784)]. Increases in albuminuria paralleled quartile increases in serum TG ($p<0.001$).18 In Minoo et al. 's study, microalbuminuria was more prevalent in very obese individuals than in the obese group (24.0% vs. 9.9%, $p = 0.043$) in univariate analysis.[19]

In our study, out of 100 patients, five died, and out of five patients, four had microalbuminuria, but these patients had high levels of microalbuminuria. Microalbuminuria can also predict mortality in acute myocardial infarction; in this respect, it can predict both short- and long-term mortality. Berton et al. considered microalbuminuria as an early predictor of mortality in acute myocardial infarction. The first and third-day microalbuminuria levels were highly significant, but not on the seventh day. Within the first three days, microalbuminuria was a better marker and predictor of outcome (in-hospital mortality) than echocardiography (ejection fraction) or Killip classification.[8]

CONCLUSION

The prevalence of microalbuminuria in acute myocardial infarction is 64%, with a notable association observed in the younger age groups. There was no significant difference in the occurrence of microalbuminuria between sexes. However, it is significantly associated with

dyslipidaemia, particularly elevated cholesterol and triglyceride levels, and a high body mass index. Although microalbuminuria is strongly linked to these factors, it can also occur independently of BMI, smoking status, and cholesterol levels in patients with acute myocardial infarction.

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